ART. IV.—*On the Causes of Failure in Vaccination.*

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THE evidence which has been accumulated in proof of the complete protection against the variolous contagion, conferred upon the human subject by effective vaccination, is too overwhelming and positive to admit of the possibility of doubt or cavil. Whenever, therefore, the occurrence of smallpox, whether in its modified or unmodified form, is witnessed in subjects reputed to have been vaccinated, it is very evident that from some cause or other the attempt at vaccination has in these cases entirely failed, or has been effective only to a partial extent.

A careful inquiry into the causes of the complete or partial failure of vaccination in certain cases is demanded, as well for the safety of those upon whom the operation is performed, as for the protection from smallpox of an entire community, amid which it may perchance be propagated through even those who are supposed to have been fully protected from the variolous contagion. The subject is one of the highest importance—interesting not merely to the physician, but to every one whether within or without the profession. To its investigation my attention has been directed for many years past, under circumstances peculiarly favourable to the attainment of correct conclusions. The results of my observations I beg leave to lay before the medical profession, in the hope that they may lead to the adoption of such precautions in reference to everything connected with vaccination as shall render it in all instances a sure and permanent protection against the contagion of smallpox.

The general conclusions to which I have been led, in respect to the leading causes of the failure of vaccination as a reliable preventive of variolous infection, are that, in the great majority of cases, at least, the want of success is traceable either to the employment of spurious or effete matter, or to the communication to those operated on of only a partial vaccine infection, or one of only temporary duration.

There are many causes by which vaccine matter may be rendered inactive or effete. Even after a genuine and perfect vaccine vesicle has been produced by the introduction of the most unexceptionable virus, its regular course may be interfered with by some accidental irritation, and simple inflammation set up, causing the vaccine lymph to become mixed, to a greater or less extent, with ordinary pus-globules. Should the scab, formed in such a case, be made use of for vaccinating, a sore arm will in general occur, but either no vaccine infection of the organism will be produced or only to a more or less limited extent; insufficient always to insure complete and permanent protection from the variolous poison. By the experienced and observant vaccinator, matter thus deteriorated would, of course, be readily detected, or should it have been accidentally made use of, he would find no difficulty in distinguishing the local phenomena induced by it from those of genuine vaccination. But, unfortunately, vaccination is often intrusted to careless and inexperienced operators, or to persons altogether unfamiliar with the true characteristics and regular course of the phenomena which result when vaccination is performed with genuine and efficient matter. By such, a sore arm produced by the insertion of spurious or partially effete matter, has been, I know from personal observation, not unfrequently, mistaken for those of perfect vaccination, and thus many an unfortunate individual, reputed to be protected from the smallpox, is sent forth to encounter its contagion with the liability to an attack of smallpox or of the so-called varioloid disease.

A fruitful source of imperfect vaccination is the use of vaccine matter which has become partially effete in consequence of its having been passed through the persons of a long succession of human subjects. Virus that has thus been made use of for vaccination, year after year, is always liable to become, to a greater or less degree, diminished in efficiency. This, I know, has been denied. The efficiency and characteristic properties of vaccine virus, however long it may have been in use, suffer, it is maintained, no deterioration. The virus in use at the present day, it is argued, is derived from that with which, at the commencement of the present century, the first vaccinations were performed in this country, and yet the phenomena resulting from its insertion in the human subject do not differ in any appreciable degree from those described and pictured by Jenner and the early vaccinators. It is hardly necessary to point out the fallacy of such statements. The assertion that no renewal of vaccine virus from the cow has taken place since the first introduction of vaccination in the United States is not accurate. As early as the year 1815 many of our physicians obtained new matter from its original source, to replace that which they had been in the habit of using. And this movement, to which they had been prompted by the example of certain of the physicians of Europe, was confessedly resorted to in consequence of the frequent disappointments which had been experienced in effecting a satisfactory vaccination with the matter already in use. Within the last eight or ten years I have myself had the pleasure of supplying many physicians, located in different parts of Pennsylvania, with recent matter; the greater activity of which, and the more prompt and certain manner in which its effects upon the systems of those vaccinated with it were displayed, was noticed by all who made trial of it.

I believe that sufficient proof of the loss, to a certain extent, of the prophylactic efficiency of vaccine virus, in its passage through many human constitutions, is the fact that it was not until after a number of years subsequently to the general adoption of vaccination in most parts of the world, and the entire disuse of variolous inoculation, that smallpox, especially in a more or less mitigated or modified form, again made its appearance, and prevailed in many places epidemically.

In Philadelphia, as we learn from the registers kept at the City Dispensary, during the sixteen years preceding 1802, a period when variolous inoculation was the only known protection against casual smallpox, *fifty-one deaths* from this disease took place, in a mortality from all causes of *seven hundred and one;* being a proportion of *seventy-three deaths* to the thousand; which corresponds with the most favourable European estimates.

From the commencement of the year 1807 an official registration of the deaths occurring in Philadelphia was required to be made by the Board of Health. From this registration, for the years 1807 to 1810, both inclusive, variolous inoculation being still performed to a considerable extent, we find that the entire mortality of the city amounted to *seventeen hundred and forty-four,* of which number there were *four hundred and twenty-nine* from smallpox, being a proportion of *forty* to the thousand.

In 1811 variolous inoculation was prohibited by law. From this period until the close of 1815, a period of four years, not a single death from smallpox is recorded. In 1816 the disease was introduced into the city by emigrants from Europe, and *ninety-seven* deaths are reported to have resulted from it. Some who were believed to have been protected by vaccination were also attacked by smallpox in a modified form. None of these, however, appears to have died.

In 1820, 1821, and 1822, Philadelphia was entirely exempt from smallpox. In 1823–24 the disease again made its appearance, and gave rise to a mortality amounting to 484. A large number of those who were reported to have been successfully vaccinated were attacked with a varioloid affection, approaching in its phenomena and intensity more or less nearly, in different cases, to genuine variola. Very few, proportionally, of these varioloid cases proved fatal.

From the last-mentioned date to the present time, with few and comparatively short intervals, smallpox has annually made its appearance in our midst, in some of its visitations exhibiting considerable malignancy, and spreading over a large portion of the city.

Pretty much the same history may be given of the prevalence of smallpox, during the present century, in every part of the world, especially from the period when vaccination entirely superseded the practice of variolous inoculation. Thus we perceive that the vaccine virus, which Jenner and his immediate followers derived directly from the cow, conferred for many years a prophylactic influence upon the human system, which in all cases was complete and permanent. After, however, the virus had been transmitted through a long series of human organisms, it lost more or less of its protective power, and they who had been subjected to its influence began again to exhibit a liability to the variolous contagion; this liability increasing in proportion to the remoteness from the cow of the matter employed in vaccination. This fact is most strikingly evinced by the very extensive series of revaccinations that have been practised yearly, from 1832 to the present time, among the soldiers of the Prussian army.

That the vaccine virus does in time lose some portion at least of its activity, and of the promptness and intensity of its action upon the human organism, is very fully shown by the fact that when the matter taken direct from the cow is made use of for vaccination, a much more decided and intense action is produced than that which results from the use of matter that has already passed through several human systems; the extent and intensity of the action produced invariably diminishing, within given limits, in proportion to the number of times the matter has been employed in vaccination. I have repeatedly seen the insertion into a child's arm of vaccine matter taken direct from the cow to be followed, about the fifth or sixth day after the operation, by more or less fever, by painful red streaks running in the direction of the nearest lymphatic glands, by great soreness, swelling, hardness, and redness of the glands of the axilla, and, in some instances, even by the occurrence of several true vaccine vesicles, most usually in the vicinity of the place of vaccination, but sometimes on remote parts of the body also.

There may be other causes of deterioration, besides those referred to, to which the vaccine virus is liable, that have not yet been detected. Among these will be found to be, I suspect, certain diseases of the skin existing in the individual from whom the matter is taken, at the period of vaccination, or during the formation, or in the progress to desiccation of the resulting vesicle.

The second cause I have assigned in explanation of the failure of vaccination as a preventive of smallpox is a deficiency in the extent of the vaccine infection imparted to the system.

The necessity of a certain intensity in the impression made upon the living organism by the insertion of vaccine virus, in order to secure to it perfect and permanent protection from variolous contagion, is established by too large an amount of indisputable facts to permit of its being any longer called in question.

The attempt at adequate vaccine infection may be defeated by the employment of effete virus, or of virus of which the specific qualities have become impaired, or worn out, if I may be allowed to use the expression, by a long series of transmissions through different human subjects.

But there are other sources of incomplete vaccination which have heretofore been in a great measure overlooked. The chief of these is an inaptitude in certain constitutions to the reception of the vaccine infection. The existence of this inaptitude, which may be either partial in extent and temporary in duration, or complete and permanent, will prevent the insertion of even the most active vaccine virus from conferring upon the human organism other than a very imperfect and more or less evanescent protection against the variolous poison. It is a well-known fact that many children cannot be made to undergo the vaccine infection until after the repeated insertion into their arms of matter of which the efficiency had been fully tested upon other subjects. I have known, in several instances, that children, in whom every attempt made to vaccinate them has failed, were very fully exposed, in after life, to the contagion of smallpox, without contracting the disease. One child, in whom vaccination was attempted, by myself and others, eight times, at different intervals, without success, was finally inoculated, by a physician in a neighbouring State, with variolous matter, but without the occurrence of the slightest symptom of smallpox locally or constitutionally. In such cases the inaptitude to vaccine infection is complete and apparently permanent. Most generally, however, the inaptitude is only partial and temporary, enabling the individual to resist, under ordinary circumstances and for a longer or shorter period, the contagion of smallpox; but when exposed to it in the more concentrated and virulent forms under which it presents itself in certain localities and during some of its epidemic visitations, the resistance is not sufficient to repel entirely its influence, and then there occurs either an attack of modified smallpox, or even perhaps of the disease in its unmodified form. In other cases the prophylaxis will continue perfect for a time, but will be finally overcome by repeated exposures to the variolous contagion.

Many experienced vaccinators in Europe deny that by vaccinating at a single spot, so as to produce only a single vaccine vesicle, the system can be placed under the vaccine influence to an extent sufficient to secure it fully and permanently from the contagion of smallpox. They recommend that, in every instance, the vaccine virus be introduced at two, three, or more points, in order to produce as many well-developed vesicles. In the official instructions to vaccinators, issued by the Central Vaccine Board of Great Britain, it is especially enjoined upon the operator to secure in every vaccination from four to five good-sized vesicles. By most of the German vaccinators it is considered, I believe, that at least three separate insertions of virus are necessary in order to secure to the vaccinated the fullest amount of protection from smallpox.

Mr. Simon, in the report of the English General Board of Health, furnishes a series of statistics which would seem to prove most unquestionably that a very strict connection exists between the number and quality of the vaccine cicatrices observed upon the person of an individual, and the protection that has been imparted to him against at least any severe or fatal attack of smallpox.

The following is the result of the observations made by Mr. Simon during a period of twenty-five years, in nearly six thousand cases of smallpox occurring in those who had been vaccinated.

In every hundred cases of smallpox contracted after reputed vaccination, in patients upon whose persons *no vaccine cicatrix* could be detected, twenty-two, or about one-fifth, proved fatal.

In every hundred cases, occurring in those who presented *one well-marked vaccine vesicle,* only four, or one twenty-fifth, died; when, however, the single cicatrix was only slightly marked, the percentage of deaths amounted to twelve.

In every hundred cases, occurring in patients who had *two well-defined vaccine cicatrices,* the number of deaths scarcely amounted to three; but when the two cicatrices were only slightly developed, the percentage of deaths reached as high as seven.

In every hundred cases, occurring in patients who had *three well-defined vaccine cicatrices,* the average mortality fell below two; while in those who had *four or more good cicatrices,* the percentage of deaths from small-pox did not amount to one.

In a series of five hundred revaccinations carefully performed under my own immediate observation, there were eighty-one of the patients who, though reputed to have been vaccinated, presented upon their bodies no trace of a vaccine cicatrix. Seventy-six presented small and very imperfect cicatrices, and and seventy-nine those of a tolerably perfect character; while, in the remaining two hundred and sixty-four, the cicatrices were well defined, presenting all the characteristics of those which result from genuine and successful vaccination. In only ten of the patients did there exist more than one cicatrix. In seven of these there were two, and in three, three cicatrices on each individual. In all of the ten cases the cicatrices were well defined.

Of the eighty-one cases in which no cicatrix was present, the vaccination performed by me succeeded perfectly in all. It could not be distinguished in any respect from that performed in the unprotected. The same thing occurred in thirty-four of the cases where the cicatrices were very obscure and defective, while in the remaining forty-two cases, and in all of the seventy-nine of those with less defective cicatrices, the insertion of matter was followed, about the fourth day, by a vesicle more or less imperfect in appearance, with, for the most part, a faint, small, irregular areola. The crust, which formed by about the ninth or tenth day, though sometimes rather earlier, but seldom much later, was of a dirty yellow or light amber colour, thin and corrugated. In the remaining cases, the attempt at vaccination was followed in a day or two, by some inflammation, a slight, circumscribed, papular elevation, at the apex of which there soon appeared a small collection of whitish pus, which drying, by the end, at the furthest, of the tenth or twelfth day, gave rise to a small, very thin, yellow scab. In some cases all the local phenomena produced by the attempt at vaccination were over by the sixth day. No permanent cicatrix remained. The vaccine matter used by me in the foregoing cases was only five removes from the cow.

The whole of the patients revaccinated as above were under nineteen years of age. The youngest was over ten years, and the oldest eighteen years, five months. The shortest time which was reported to have elapsed from the period of the primary vaccination was over nine years, and the longest eighteen years. No relation was observed to exist between the appearance of the cicatrices on the arm, nor the more or less perfect success of the secondary vaccination, and the age of the patient or the period which had elapsed since the vaccination was said to have been performed.

In view of the many causes by which the attempt at vaccination, in the first instance, may be rendered unsuccessful, or only in part successful, and of the very great difficulty of avoiding most of these causes of failure, even by the utmost caution and foresight, the propriety, if not the absolute necessity of a resort to revaccination demands the earnest consideration of every practitioner. It is, in fact, the only reliable test of the entire success of the first operation; the only means to insure the safety of the patient from an attack of smallpox.

It is believed that in every doubtful case an early resort to a second or even third insertion of vaccine matter, of the purity and activity of which we are well assured, should be insisted upon, in order to complete the infection of the system, if it had not been accomplished by the first operation. Nor should we stop here. The examination of a very extended series of well authenticated statistics has convinced me that, in many cases, the protection attempted to be conferred upon the human organism by the primary vaccination is at best but temporary—and can be rendered permanent only by a second, or, in some few instances, by repeated revaccinations. Hence it would seem to be demanded in all cases, without exception, as a proper precautionary measure, that vaccination be repeated after a proper interval, to insure the complete infection of the system—to endue it with the due amount of protection against the variolous poison.

Were such a course to be invariably and systematically pursued, and, in addition, were general revaccination to be resorted to, and carried thoroughly out, in every instance when smallpox makes its appearance in a city, village, town, or neighbourhood, not only would the spread of the disease be prevented, but the possibility of its future occurrence be very effectually guarded against. Unless such precautionary measures against the occurrence of smallpox are adopted and promptly and faithfully executed in every community, it is impossible to hope for the utter exclusion, now and henceforward, of this loathsome and destructive disease.